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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/520,754	01/10/2005	Anne Marie Jeanne Bouillot	PF4879USW	4849

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EXAMINER	
MABRY, JOHN	

ART UNIT	PAPER NUMBER
1609	

MAIL DATE	DELIVERY MODE
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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/520,754	BOUILLOT ET AL.	
	Examiner	Art Unit	
	John Mabry	1609	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *10 January 2005*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-12 and 15* is/are pending in the application.

4a) Of the above claim(s) *15* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-12* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *1/10/05*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Election/Restrictions

Restriction is required under 35 U.S.C. 121 and 372.

This application contains the following inventions or groups of inventions which are not so linked as to form a single general inventive concept under PCT Rule 13.1.

In accordance with 37 CFR 1.499, applicant is required, in reply to this action, to elect a single invention to which the claims must be restricted.

I. Claims 1-10 and 12 are drawn to compounds and pharmaceutical compositions of formula I wherein Ar_1=phenyl, E=C_4 alkylene, X=-NR_2CO-, Ar_2=phenyl and Ar_3=phenyl. A further election of single disclosed species is required.

II. Claims 1-12 are drawn to compounds and pharmaceutical compositions of formula I wherein Ar_1=phenyl fused by C_6 cycloalkyl, E=C_4 alkylene, X=-NR_2CO- and Ar_2=phenyl and Ar_3=phenyl. A further election of single disclosed species is required.

III. Claims 1-10 and 12 are drawn to compounds and pharmaceutical compositions of formula I wherein Ar_1=phenyl, E=C_4 alkylene, X=- NR_2CO-, Ar_2=thiazoyl and Ar_3=phenyl. A further election of single disclosed species is required.

IV. Claims 1-12 are drawn to compounds and pharmaceutical compositions of formula I wherein Ar_1=phenyl fused by C_6 cycloalkyl, E=C_4 alkylene, X=- NR_2CO- Ar_2=thiazoyl and Ar_3=phenyl. A further election of single disclosed species is required.

V. Claims 1-10 and 12 are drawn to compounds and pharmaceutical compositions of formula I wherein Ar_1=phenyl, E=C_4 alkylene, X=- NR_2CO-, Ar_2=oxazoyl and Ar_3=phenyl. A further election of single disclosed species is required.

VI. Claims 1-10 and 12 are drawn to compounds and pharmaceutical compositions of formula I wherein Ar_1=phenyl fused by C_6 cycloalkyl, E=C_4 alkylene, X=- NR_2CO- Ar_2=oxazoyl and Ar_3=phenyl. A further election of single disclosed species is required.

VII. Claims 1-12 are drawn to compounds and pharmaceutical compositions of formula I that are not encompassed by Groups I-VI. An election of species is required. A further election of single disclosed species is required.

VIII. Claim 15 is drawn to a method of treatment of a condition resulting from elevated circulating levels of LDL-cholesterol in a mammal by one of the groups I-VII. A species election is required. A further election of single disclosed species is required.

The claims herein lack unity of invention under PCT rule 13.1 and 13.2 since, under 37 CFR 1.475(a) Group I -Group XII lack unity of invention since under 37 CFR 1.475:

> Where a group of inventions is claimed in an application, the requirement of unity of invention shall be fulfilled only when there is a technical relationship among those inventions involving one or more of the same or corresponding special technical features...those technical features that define a contribution which each of the claimed inventions, considered as a whole, makes over the prior art.

The technical feature corresponding to group I, formula I, is the substituted piperidinyl scaffold, wherein Ar_1=phenyl, E=C_4 alkylene, X=-NR_2CO-, Ar_2=phenyl and Ar_3=phenyl. Group II contains cyclohexyl-fused Ar_1 of formula I, wherein Ar_1=phenyl fused by C_6 cycloalkyl, E=C_4 alkylene, X=-NR_2CO- and Ar_2=phenyl and Ar_3=phenyl. Group III contains wherein Ar_2 is thiozoyl of formula I, wherein Ar_1=phenyl, E=C_4 alkylene, X=- NR_2CO-, Ar_2=thiazoyl and Ar_3=phenyl as the special technical feature. The technical feature corresponding to group IV, formula I, is wherein Ar_1=phenyl fused by C_6 cycloalkyl, E=C_4 alkylene, X=- NR_2CO- Ar_2=thiazoyl and Ar_3=phenyl. The special technical feature corresponding to group V, formula I, is wherein Ar_1=phenyl, E=C_4 alkylene, X=- NR_2CO-, Ar_2=oxazoyl and Ar_3=phenyl. Group VI contains cyclohexyl-fused Ar1 of formula I, wherein Ar_1=phenyl fused by C_6 cycloalkyl, E=C_4

alkylene, X=- NR_2CO- Ar_2=oxazoyl and Ar_3=phenyl. Group VII consists of all other structures corresponding to formula I that are not emcompassed by the special technical features of Groups I-VII. These ring systems are not considered equivalent.

The technical feature corresponding to group VIII is a method of treating a condition resulting from elevated circulating levels of LDL-cholesterol in a mammal according to compounds of formula I of any one of the Groups I-VII.

Therefore the above claims, are not so linked as to form a single general inventive concept and there is a lack of unity of invention because they lack a common core structure and the technical features present fail to define a contribution over the prior art. Accordingly, unity of invention is considered to be lacking and restriction of the invention in accordance with the rules of unity of invention is considered to be proper.

> Therefore, since the claims do not relate to a single general inventive concept under PCT Rule 13.1 and lack the same or corresponding special technical features, the claims lack unity of invention and should be limited to only one invention.

Restriction for examination purposes as indicated is proper because all these inventions listed in this action are independent or distinct for the reasons given above and there would be a serious search and examination burden if restriction were not required because one or more of the following reasons apply:

(a) the inventions have acquired a separate status in the art in view of their different classification;

(b) the inventions have acquired a separate status in the art due to their recognized divergent subject matter;

(c) the inventions require a different field of search (for example, searching different classes/subclasses or electronic resources, or employing different search queries);

(d) the prior art applicable to one invention would not likely be applicable to another invention;

(e) the inventions are likely to raise different non-prior art issues under 35 U.S.C. 101 and/or 35 U.S.C. 112, first paragraph.

Applicant is advised that the reply to this requirement to be complete must include (i) an election of a invention to be examined even though the requirement may be traversed (37 CFR 1.143) **and (ii) identification of the claims encompassing the elected invention.**

The election of an invention may be made with or without traverse. To reserve a right to petition, the election must be made with traverse. If the reply does not distinctly and specifically point out supposed errors in the restriction requirement, the election shall be treated as an election without traverse. Traversal must be presented at the time of election in order to be considered timely. Failure to timely traverse the requirement will result in the loss of right to petition under 37 CFR 1.144. If claims are added after the election, applicant must indicate which of these claims are readable on the elected invention.

If claims are added after the election, applicant must indicate which of these claims are readable upon the elected invention.

Should applicant traverse on the ground that the inventions are not patentably distinct, applicant should submit evidence or identify such evidence now of record

showing the inventions to be obvious variants or clearly admit on the record that this is the case. In either instance, if the examiner finds one of the inventions unpatentable over the prior art, the evidence or admission may be used in a rejection under 35 U.S.C. 103(a) of the other invention.

Election

During a telephone conversation with Lorie Ann Morgan on August 22, 2007, a provisional election was made without traverse to prosecute the invention of Group I, claims 1-12. The species elected is compound Example 1 on page 37 of specification. It is also noted that a request for rejoinder has been expressly withdrawn, thus claim 15 is withdrawn from further consideration by the examiner, 37 CFR 1.142(b), as being drawn to a non-elected invention. Affirmation of this election must be made by applicant in replying to this Office action.

Rejoinder Advisory

The examiner has required restriction between product and process claims. Where applicant elects claims directed to the product, and the product claims are subsequently found allowable, withdrawn process claims that depend from or otherwise require all the limitations of the allowable product claim will be considered for rejoinder. All claims directed to a nonelected process invention must require all the limitations of an allowable product claim for that process invention to be rejoined.

In the event of rejoinder, the requirement for restriction between the product claims and the rejoined process claims will be withdrawn, and the rejoined process

claims will be fully examined for patentability in accordance with 37 CFR 1.104. Thus, to be allowable, the rejoined claims must meet all criteria for patentability including the requirements of 35 U.S.C. 101, 102, 103 and 112. Until all claims to the elected product are found allowable, an otherwise proper restriction requirement between product claims and process claims may be maintained. Withdrawn process claims that are not commensurate in scope with an allowable product claim will not be rejoined. See MPEP § 821.04(b). Additionally, in order to retain the right to rejoinder in accordance with the above policy, applicant is advised that the process claims should be amended during prosecution to require the limitations of the product claims. **Failure to do so may result in a loss of the right to rejoinder**. Further, note that the prohibition against double patenting rejections of 35 U.S.C. 121 does not apply where the restriction requirement is withdrawn by the examiner before the patent issues. See MPEP § 804.01.

Applicant is advised that the reply to this requirement to be complete must include (i) an election of a species or invention to be examined even though the requirement be traversed (37 CFR 1.143) and (ii) identification of the claims encompassing the elected invention.

The election of an invention or species may be made with or without traverse. To reserve a right to petition, the election must be made with traverse. If the reply does not distinctly and specifically point out supposed errors in the restriction requirement, the election shall be treated as an election without traverse.

Should applicant traverse on the ground that the inventions or species are not patentably distinct, applicant should submit evidence or identify such evidence now of

record showing the inventions or species to be obvious variants or clearly admit on the record that this is the case. In either instance, if the examiner finds one of the inventions unpatentable over the prior art, the evidence or admission may be used in a rejection under 35 U.S.C.103(a) of the other invention.

Applicant is reminded that upon the cancellation of claims to a non-elected invention, the inventorship must be amended in compliance with 37 CFR 1.48(b) if one or more of the currently named inventors is no longer an inventor of at least one claim remaining in the application. Any amendment of inventorship must be accompanied by a request under 37 CFR 1.48(b) and by the fee required under 37 CFR 1.17(i).

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 1-12 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Regarding claim 1, the phrase "such as" renders the claim indefinite because it is unclear whether the limitations following the phrase are part of the claimed invention. See MPEP § 2173.05(d).

The term "acyl" in claim 1 is a relative term which renders the claim indefinite. The term "acyl" is not defined by the claim, the specification does not provide a

standard for ascertaining the requisite degree, and one of ordinary skill in the art would not be reasonably apprised of the scope of the invention. Applicant attempted to define the term acyl as aliphatic or cyclic hydrocarbons attached to a carbonyl group through which the substituent bonds, such as acetyl (see page 7, lines 31 and 32). The Examiner interprets this to define an indefinite terms with another indefinite term. What exactly does Applicant mean by statement "through which the substituent bonds"? What exactly does Applicant mean by the term acyl?

> The following is a quotation of the first paragraph of 35 U.S.C. 112:
>
> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 1-12 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for "salts", does not reasonably provide enablement for solvates. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make the invention commensurate in scope with these claims.

Claims 1-12 are drawn to "solvates", but the numerous examples presented all failed to produce a solvate. These cannot be simply willed into existence. As was stated in *Morton International Inc. v. Cardinal Chemical Co.*, 28 USPQ2d 1190 "The specification purports to teach, with over fifty examples, the preparation of the claimed

compounds with the required connectivity. However ... there is no evidence that such compounds exist... the examples of the '881 patent do not produce the postulated compounds... there is ... no evidence that such compounds even exist." The same circumstance appears to be true here: there is no evidence that solvates of these compounds actually exist; if they did, they would have formed. Hence, applicants must show that solvates can be made, or limit the claims accordingly.

Claims 1-12 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for "salts", does not reasonably provide enablement for "prodrugs". The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make the invention commensurate in scope with these claims.

The nature of the invention in the instant case has claims which embrace aryl piperidine compounds. The scope of "prodrug" is not adequately enabled. Applicants provide no guidance as how the compounds are made more active *in vivo*. The choice of a "prodrug" will vary from drug to drug. Therefore, more than minimal routine experimentation would be required to determine which prodrugs will be suitable for the instant invention.

The instant compounds of formula (I) wherein the prodrugs are not described in the disclosure in such a way the one of ordinary skill in the art would no how to prepare the various compounds suggested by said claims. In view of the lack of direction provided

in the specification regarding starting materials, the lack of working examples, and the general unpredictability of chemical reactions, it would take an undue amount of experimentation for one skilled in the art to make the claimed compounds and therefore practice the invention.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (a) the invention was known or used by others in this country, or patented or described in a printed publication in this or a foreign country, before the invention thereof by the applicant for a patent.
>
> (e) the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effects for purposes of this subsection of an application filed in the United States only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language.

The applied reference has a common assignee with the instant application. Based upon the earlier effective U.S. filing date of the reference, it constitutes prior art under 35 U.S.C. 102(e). This rejection under 35 U.S.C. 102(e) might be overcome either by a showing under 37 CFR 1.132 that any invention disclosed but not claimed in the reference was derived from the inventor of this application and is thus not the invention "by another," or by an appropriate showing under 37 CFR 1.131.

Claims 1-12 are rejected under 35 U.S.C. 102(a) and (e) as being anticipated by Bouillot et al (WO 02/055497 A1, US equivalent – US 2004/0147557 A1).

The instant Application claims compounds of Formula I, wherein Ar_1=phenyl substituted by $-O(CH_2)_2OR^2$ where R^2=H, E=C_4 alkylene, X=$-NR_2CO-$, Ar_2=phenyl substituted with $-CH_3$ and Ar_3=phenyl substituted with -OH.

Bouillot et al discloses compounds of Formula I, wherein Ar_1=phenyl $-O(CH_2)_2R^2$ where R^2=H where each alkylene group may additionally incorporate an oxygen in the chain with the proviso that there are at least two carbons between any chain heteroatom, E=C_4 alkylene, X=$-NR_2CO-$, Ar_2=phenyl substituted with $-CH_3$ and Ar_3=phenyl substituted with –OH (see page 7, line 1 – page 8, line 7).

Obvious double patent rejections were considered to the instant application using references US 2004/0077654 A1 and US 2004/0147557 A1. However, the referenced applications were abandoned by application prior to the examination of this application.

The prior art made of record and not relied upon is considered pertinent to applicant's disclosure. WO 02/055495 A1, WO 02/055496 A1, and US 2004/0077654 A1 by Bouillot et al disclose species of formula I as described in above rejection.

Conclusion

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only.

For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Any inquiry concerning this communication or earlier communications from the examiner should be directed to John Mabry whose telephone number is (571) 270-1967. The examiner can normally be reached on M-F from 9am to 5pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Jeffrey Stucker, can be reached on (571) 272-0911. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

jm

JM

R Desai 8/30/07

RITA DESAI
PRIMARY EXAM